UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF MISSOURI
EASTERN DIVISION

IN RE NUVARING® PRODUCTS LIABILITY LITIGATION	)	Case No. 4:08-MD-1964 RWS
	)	ALL CASES

MEMORANDUM AND ORDER

Plaintiffs challenge the qualifications of two of Defendants' ("Organon's") experts, Drs. Titia Mulders and Hans Rekers, to present expert testimony. Plaintiffs ask me to find, as a matter of law, that these witnesses are so unqualified that all of their opinions should be excluded from being tested by any cross-examination at trial, being weighed by any jury, or even limited in any respect by any trial judge. For the reasons stated below, the motions will be granted in part and denied in part**.**

I. BACKGROUND

This multi-district litigation (MDL) relates to the manufacture, marketing, and sale of the prescription pharmaceutical known as NuvaRing. NuvaRing, which is manufactured, marketed, and sold by Organon, is a member of a class of prescription drugs known as combined hormonal contraceptives, which contain an estrogen and a progestin component. Unlike oral CHCs, NuvaRing takes the form of a flexible ring which releases hormones over the course of treatment. The ring is vaginally inserted by women for birth control. Each month, the ring is removed and a new ring is inserted.

CHCs contain an estrogen, typically ethinyl estradiol ("EE"), and a progestin. The "generation" of CHC depends upon the type of progestin. Each "generation" of CHC typically includes the following progestins: first-generation contains norethynodrel; second-generation

contains levonorgestrel; and third-generation CHCs contain desogestrel, gestodene, or norgestimate. NuvaRing uses the active metabolite of desogestrel, etonogestrel, and is therefore considered a third-generation progestin.

Plaintiffs allege that the progestin used on the ring, etonogestrel, has been linked to an undisclosed increased risk of venous thromboembolism, including both deep vein thrombosis and pulmonary embolism.[1] Plaintiffs allege they have been injured by the use of NuvaRing and have asserted the following claims: strict products liability for defective manufacturing, defective design, failure to test, and inadequate warnings; breach of express / implied warranties; and negligence.

Plaintiffs contend that two of Organon's experts, Dr. Titia Mulders and Dr. Hans Rekers, fail to meet the requirements for admissible expert testimony under Federal Rule of Evidence 702 and Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579 (1993). Specifically, Plaintiffs seek to preclude all testimony by these individuals by contending that their proffered opinions are beyond the scope of these witnesses' expertise and qualifications.

II. LEGAL STANDARD

Federal Rule of Evidence 702 governs the admissibility of expert testimony. Rule 702 provides:

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.

[1] Venous thromboembolism is a blood clot that forms within a vein. Deep vein thrombosis is a blood clot that forms in a vein not externally visible, typically in the veins of the lower extremities. A pulmonary embolism forms when part or all of a blood clot breaks free and lodges in one of the lungs. These conditions have varying severity and can be life threatening.

Under Rule 702, the trial judge acts as a "gatekeeper" screening evidence for relevance and reliability. Daubert, 509 U.S. at 589. "Rule 702 reflects an attempt to liberalize the rules governing the admission of expert testimony. The rule clearly is one of admissibility rather than exclusion." Lauzon v. Senco Prods., Inc., 270 F.3d 681, 686 (8th Cir. 2001) (internal quotations and citations omitted).

The party proffering an expert witness must establish by a preponderance of the evidence that the witness testimony is admissible. Daubert, 509 U.S. at 592 & n.10 (citing Rule 104(a)). A district court applies a three-part test when screening expert testimony under Rule 702:

> First, evidence based on scientific, technical, or other specialized knowledge must be useful to the finder of fact in deciding the ultimate issue of fact. This is the basic rule of relevancy. Second, the proposed witness must be qualified to assist the finder of fact. Third, the proposed evidence must be reliable or trustworthy in an evidentiary sense, so that, if the finder of fact accepts it as true, it provides the assistance the finder of fact requires.

Polski v. Quigley Corp., 538 F.3d 836, 839 (8th Cir. 2008) (quoting Lauzon, 270 F.3d at 686).

The broad and generally stated test for determining the qualifications of a given witness to testify as an expert is whether his knowledge of the subject matter is such that his opinion will most likely assist the trier of fact in arriving at the truth. Holmgren v. Massey-Ferguson, Inc., 516 F.2d 856, 857–58 (8th Cir. 1975) (citing Moran v. Ford Motor Co., 476 F.2d 289 (8th Cir. 1973); Chicago Great Western Ry. Co. v. Beecher, 150 F.2d 394 (8th Cir. 1945)).

"[T]he rejection of expert testimony is the exception rather than the rule." Robinson v. GEICO General Ins. Co., 447 F.3d 1096, 1100 (8th Cir. 2006) (citing Fed. R. Evid. 702 advisory comm. note). "Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence." Daubert, 509 U.S. at 596.

III. ANALYSIS

A. Motion to Exclude Testimony of Titia Mulders, Ph.D.

1. Dr. Mulders's Background

Dr. Mulders has a Master's degree in biomedical sciences and a Ph.D. in clinical pharmacology and toxicology from Leiden University. (Doc. 1373; Exh. 1, hereinafter "Mulders Decl.," at ¶¶ 4, 6). Her coursework included classes in epidemiology, clinical medicine, oncology, biology, and cell differentiation. (Id. at ¶ 7).

Since receiving her Ph.D. in 1994, Dr. Mulders has worked in Organon's drug development department with a focus on hormonal contraceptives and hormone-based fertility products. (Id. at ¶ 7). From 1997 through 2000, she chaired the NuvaRing Clinical Development Team overseeing the NuvaRing Phase III clinical trials. (Id. at ¶ 9). In 2000, Dr. Mulders became chair of the NuvaRing Project Team, which was responsible for regulatory matters, clinical research and development, pharmaceutical and chemical development, non-clinical research and product life-cycle management. (Id. at ¶ 10).

2. Dr. Mulders's Proffered Expert Testimony

Organon proffers Dr. Mulders to testify as to twenty-eight topics. Plaintiffs seek to exclude the testimony of Dr. Mulders on the grounds that Organon failed to meet its burden of demonstrating her qualifications. Organon responds that it does not regard Dr. Mulders's opinions as traditional expert testimony, but rather as factual in nature and, insofar as her opinions derive from scientific knowledge, Dr. Mulders possesses the requisite qualifications to give those opinions. Rather than examining each of Dr. Mulders's twenty-eight opinions, the parties address Dr. Mulders' qualifications in broad categories: a) Food and Drug Administration

regulatory matters and the adequacy of the NuvaRing label; b) epidemiology; and c) the risk and benefits of NuvaRing.

As a preliminary matter, I note that many of Dr. Mulders's testimonial topics are a mix of "specialized knowledge," which is subject to Rule 702 and Daubert, and lay testimony, which is subject to Rule 701.[2] Plaintiffs' motion only challenges Dr. Mulders's testimony under Rule 702.

a) FDA Regulatory Matters and the Adequacy of the NuvaRing Label

Organon argues that Dr. Mulders's experience at Organon qualifies her to testify regarding FDA regulations and the NuvaRing label compliance with such regulations. However, Organon fails to articulate specific experiences of Dr. Mulders which qualifies her to testify on these areas. Dr. Mulders testified that she chaired the NuvaRing Project Team, which included a regulatory sub-team.[3] (Mulders Decl. ¶ 10; Doc. 1314, Exh. 3, Titia Mulders Depo. April 6, 2011, at 406–07). Dr. Mulders testified that each sub-team has its own responsibility within its respective disciplines. (Doc. 1314, Exh. 3 at 406–07). It is true that Dr. Mulders's team was involved in submissions to and communications with the FDA. (Mulders Decl. ¶¶ 20–26). However, Dr. Mulders admitted that she is not a regulatory expert in the United States and deferred questions to her regulatory colleagues. For example, the following exchange occurred during one of her depositions:

[2] If a witness is not testifying as an expert, testimony in the form of an opinion is limited to one that is: (a) rationally based on the witness's perception; (b) helpful to clearly understanding the witness's testimony or to determining a fact in issue; and (c) not based on scientific, technical, or other specialized knowledge within the scope of Rule 702.

[3] The Project Team also included clinical development, chemical pharmaceutical and non-clinical teams, among others. (Doc. 1314, Exh. 3, Titia Mulders Depo., April 6, 2011, at 406–07).

> Q: Do any of these clinical reports that we will look at today in the form that they exist, are they given to the FDA?
> A: So I'm not a regulatory expert in the United States. I know that we have an obligation for full disclosure. Whether that also implies that the clinical reports have been provided to the FDA, I wouldn't know. I think you have to ask that to one of my regulatory colleagues.

(Doc. 1314, Exh. 3, Titia Mulders Depo. Apr.6, 2011, at 394).

I find that Organon fails to establish the qualifications of Dr. Mulders to testify regarding FDA regulatory matters and the adequacy of the NuvaRing label. Plaintiffs' motion to exclude Dr. Mulders regarding this category of testimony is granted. Dr. Mulders may, of course, testify as to the factual development of NuvaRing, including which studies Organon relied upon when submitting the NuvaRing label to the FDA.

b) Epidemiology

Organon maintains that Dr. Mulders's experience as the lead scientist on the team responsible for the research and development, regulatory approval, and labeling of NuvaRing qualifies her to offer opinions about the epidemiologic data that informed the company's decisions on those issues. However, Dr. Mulders testified that she was not an expert in epidemiology. (Doc. 1314, Exh. 4, Titia Mulders Depo., June 28, 2012, at 346) ("No. I already mentioned before I'm not an expert in epidemiology."). Dr. Mulders further testified that when presented with epidemiological studies, she relied upon experts within the company for guidance as to how to read the information:

> Q: And when you say that you read all the papers about the epidemiology of combined hormonal contraceptives, that's your epidemiological training as well, correct, you read the papers?
> A: No. I said that, obviously, as of the mid '90s, there has been – several papers have been published and we also had discussions with experts within the company as to how to read the information from the various sources that become available to us.

(Id. at 345).

While Dr. Mulders may have obtained some second-hand experience in epidemiology during her work on NuvaRing, I find that Organon has failed to show that Dr. Mulders possesses the qualifications necessary to give expert testimony pertaining to epidemiology. Plaintiffs' challenge to this category of testimony is granted**.**

c) Risks and Benefits of NuvaRing

Dr. Mulders is a trained and credentialed pharmacologist. To the extent that she relies upon that expertise to discuss the risks and benefits of NuvaRing, I find her qualified. However, to the extent she wishes to discuss the risks and benefits of NuvaRing relevant to other disciplines, her qualifications are less clear.

Beyond the conclusory assertion that Dr. Mulder's role as clinical researcher and Global Project Team chair qualifies her to offer opinions on the risks and benefits of NuvaRing, Organon fails to assert any particular education, experience, or other qualifications that might support Dr. Mulders's testimony. Although Organon cites twenty studies that Dr. Mulders oversaw during her work on NuvaRing, Dr. Mulders admitted that she only authored four. (Mulders Decl. ¶ 13). The record does not reflect which of the twenty articles Dr. Mulders authored. Moreover, as noted above, Dr. Mulders testified that she relied on the expertise of the individual sub-teams during her tenure at Organon. Although she is being offered as an expert on the hemostatic profile of NuvaRing, Dr. Mulders repeatedly disclaimed expertise in and deferred questions related to hemostasis, VTEs and cardiovascular risk. Take the following testimony, for example:

> I am not a hemostasis expert. I would—if you want to discuss the individual parameters within the hemostasis system, I would want to refer—to defer to Hans Rekers, my Medical Doctor colleague, who's much more experienced in this specific area than I am.

(Doc. 1314, Exh. 5, Titia Mulders Depo., July 27, 2010, at 727).

> Q: So fibrin formation is what? Is that, again, an indicator of clotting?
> A: I'm not an expert on the hemostasis system, so I think if you would want to have an in-depth discussion on all the hemostasis possibilities, I would want to defer to, for example, my colleague Hans Rekers. I think the hemostasis system is a quite complicated system. I'm not an expert on the hemostasis system.
> Q: Okay. That's fine. You – that's fine. But you wrote about it in this report.
> A: The hemostasis study in itself was not a study that was conducted under my personal responsibility.
> . . . .
> . . . But as I mentioned before, the studies are being conducted by a team of experts.

(Doc. 1314, Exh. 3, Titia Mulders Depo., April 6, 2011, at 584–85).

> I think, I mean, if you want to talk about studies that are designed to evaluate the cardiovascular risks associated with the use of combined hormonal contraceptives, I think I would want to defer to my colleague Hans Rekers because he is an expert in the field of observational types of studies. And I think also he is an expert on all the different papers that have been published on this specific topic.

(Doc. 1314, Exh. 6, Titia Mulders Depo., April 5, 2011, at 190–91).

> I think I already mentioned before, if you want to have an in-depth discussion about all medical—or all conditions that lead to venous thromboembolism, that is the area of expertise of my colleague Hans Rekers. . . .

(Id. at 241).

Nor is Dr. Mulders a medical doctor. (See generally Doc. 1314, Exh. 7, Mulders C.V.; see also Doc. 1446, Exh. 4, Titia Mulders Depo., July 27, 2010, at 645 (deferring discussion on health risks to her medical colleagues)).

As a result, I find that Organon has failed to establish the qualifications of Dr. Mulders to testify broadly as to the risks and benefits of NuvaRing and combined hormonal contraceptives in general. I do, however, find Dr. Mulders qualified to discuss the benefits and risks of NuvaRing insofar as they relate to its pharmacokinetic and pharmacodynamics profiles. Plaintiffs' motion as to this category of testimony will be granted in part.

B. Motion to Exclude Testimony of Hans Rekers, M.D.

1. Dr. Rekers's Background

Dr. Rekers received an M.D. from the University of Amsterdam in 1982. Over the past twenty-five years, Dr. Rekers has worked for Organon and Merck. His roles with these pharmaceutical companies have involved design and execution of phase III and IV clinical trials, management of medical defense of third-generation hormonal contraceptive litigation, management of product safety and efficacy issues teams, and development of epidemiological studies. Dr. Rekers has edited, authored, or co-authored eighteen books and articles on varying topics related to pharmaceuticals and hormonal contraceptives in particular. (Doc. 1312, Exh. 5, Hans Rekers C.V.).

2. Dr. Rekers's Proffered Expert Testimony

Organon intends to present testimony from Dr. Rekers on more than fifty topics. As with Dr. Mulders, "Defendants do not regard Dr. Rekers' expected testimony as traditional expert opinion testimony; but rather, as factual, historical, and state of mind testimony regarding Defendants' involvement with NuvaRing . . . but which necessarily involves scientific and medical knowledge."

Rather than addressing Dr. Rekers's qualifications as they pertain to each of his opinions, the parties address the qualifications of Dr. Rekers in broad categories: epidemiology; biostatistics; the safety and efficacy of hormonal contraceptives, including pharmacological, biochemical and hematological evidence bases therefor; regulation of NuvaRing; and risks and benefits of NuvaRing and other combined hormonal contraceptives.

As with Dr. Mulders, I note that many of Dr. Rekers's testimonial topics are a mix of "specialized knowledge," which is subject to Rule 702, and lay testimony, which is subject to Rule 701. Plaintiffs' motion only challenges Dr. Rekers's testimony under Rule 702.

a) Epidemiology

Plaintiffs contend that because Dr. Rekers is not an "epidemiologist" and possesses no advanced degree or specialization in the field of epidemiology, he should be precluded from offering expert testimony in that field. Organon responds that Dr. Rekers's qualifications stem from his experience in designing and overseeing epidemiological studies and in publishing on the topic of epidemiology.

I find that Dr. Rekers is qualified to testify related to epidemiology based upon his experience in performing and overseeing epidemiological studies, reviewing and commenting upon protocols, and in coauthoring academic papers on epidemiology. (See Doc. 1440, Exh. 6, Hans Rekers Depo., June 26, 2012, at 45–46; Doc. 1312, Exh. 5, Hans Rekers C.V. at 5). Plaintiffs' challenge to Dr. Rekers's epidemiology testimony is denied**.**

b) Biostatistics

Plaintiffs argue that Dr. Rekers is unqualified to testify regarding biostatistics, because Dr. Rekers testified that he lacks expertise in statistics, does not perform statistical analyses, and relies upon others to interpret statistics. Organon responds that Dr. Rekers is not being offered as an expert on the general topic of biostatistics. Rather, Organon expects Dr. Rekers "to testify about statistical power and related methodology issues inherent in the design and interpretation of the hormonal contraceptive epidemiology." Organon maintains that Dr. Rekers is qualified to so testify based upon his personal knowledge and epidemiological research experience.

I find that Dr. Rekers lacks the qualifications necessary to give expert testimony as to the field of biostatistics. Dr. Rekers denied expertise in statistics:

> Q: This Cox regression analysis, from your perspective, can you define that for me?
> A: No, I cannot.
> Q: You cannot?
> A: I am not a statistical expert. I'm not a statistical expert, and I am not the person you should be speaking to about the finesses of a Cox regression analysis.
> . . . .
> Q: And so, without refreshing your memory and looking at Dr. Suissa's paper, you can't generally describe this spline regression analysis?
> A: No. I can tell you it takes into account duration of use in a sophisticated statistical way. But to describe it any further than that, I would really have to go into the statistics, and I feel uncomfortable in doing that, not being a statistician.

(Doc. 1440, Exh. 4, Hans Rekers Depo., April 8, 2011, at 434, 440–41).

Dr. Rekers further testified that he did not understand statistical power calculations and different methods used.

> Q: When you say it was determined that it would be best for there to be direct communication between Pierre [Verway] and the researchers on [the] TASC [study], why is it— why is it that you had a biostatistician have that discussion directly rather than you make that decision?
> A: Because these are biostatistical calculations that are made. I would be relevant to be involved in such discussions if the assumptions that go into the power calculations would be discussed, like what is the expected rate of VTE and what study have we used to come up with that expected rate of VTE that we are using in the power calculations. That would have been relevant for me to be included in.
>
> But the moment they are talking about the power calculations themselves, and different methods used, that's all mathematics and statistics, and I am not enough of a person understanding the calculations in statistics to be a significant contributor to such discussions.
> . . . .
> Q: Would I be correct in stating that you would defer to a—some other expert on— in discussing the methodology and the power calculations for this study, the TASC study?
> A: No. That is incorrect. I deferred, for the statistics of the power calculations, to Pierre Verwey and direct discussions with the ZEG team. On the methodology of the study, I did not defer anything to Pierre Verwey.

(Doc. 1440, Exh. 6, Hans Rekers Depo., June 26, 2012 at 103–105). As a result, Plaintiffs' motion to exclude Dr. Rekers's testimony as to the field of biostatistics is granted**.**

c) Safety and Efficacy of Hormonal Contraceptives including Biochemical, Hematological and Pharmacological Issues

Plaintiffs allege that Dr. Rekers lacks qualifications to opine on biochemical, hematological and pharmacological matters. Organon responds that Dr. Rekers's broad experience "in all aspects of evaluating the safety and efficacy of hormonal contraceptives" qualifies him to opine on these topics.

The form of the parties' briefs and the state of the record as a whole make it difficult to gauge the full extent of Dr. Rekers's knowledge and experience with any particular field of science. However, Dr. Rekers's *curriculum vitae* lists some co-authored papers in the challenged fields. (Doc. 1312, Exh. 5 at 5–6). I find that Dr. Rekers is qualified to testify as to the safety and efficacy of hormonal contraceptives, including opinions based in biochemistry, hematology and pharmacology. Plaintiffs' motion to exclude Dr. Rekers's testimony on these topics is denied**.**

d) Regulation of NuvaRing

Plaintiffs allege that Dr. Rekers lacks qualifications to give expert testimony pertaining to the regulation of NuvaRing. Organon responds that Dr. Rekers is not being offered to recite FDA regulations or explain drug regulations to the jury. Rather, Dr. Rekers will testify regarding the company's dealings with the FDA and other regulatory bodies, the disclosure of drug safety data in connection with NuvaRing, and actions taken by the FDA concerning NuvaRing.

Dr. Rekers's proffered opinions go far beyond the limited factual testimony that Organon represents. For example, Dr. Rekers opines that the NuvaRing label and clinical trials are consistent with FDA and other regulatory requirements. While the record indicates that Dr.

Rekers has knowledge and experience with the data provided to the FDA, there is no showing that Dr. Rekers is qualified to testify as to whether the NuvaRing label or studies comply with regulatory standards.

> Q: So if I understand it, clinical aspects of NuvaRing is within your field of expertise.
> A: It is, yes.
> Q: The labeling of NuvaRing is within your field of expertise?
> A: The clinical aspects of labeling is, yes.
> Q: When you say "clinical aspects of labeling," what do you mean?
> A: I mean the understanding of what it actually means that is stated there.
> . . . .
> Q: Doctor, one of the areas that . . . you were designated in part . . . is compliance with any and all U.S. pharmaceutical regulations.
> A: Uh-huh.
> Q: Would you be the person to give me answers regarding compliance issues in terms of FDA regulations?
> A: No, I would not.

(Doc. 1440, Exh. 7, Hans Rekers Depo., July 21, 2010, at 19–20, 405).

Organon fails to demonstrate that Dr. Rekers is qualified to present testimony regarding compliance with regulatory standards. Plaintiffs' motion to exclude Dr. Rekers's testimony related to compliance with regulatory standards is granted**.**

e) Risks and Benefits of NuvaRing and other Combined Hormonal Contraceptives

Plaintiffs argue that Dr. Rekers lacks sufficient expertise to testify regarding the risks and benefits of NuvaRing and to opine regarding prescribing decisions by physicians. Organon responds that Dr. Rekers's qualifications stem from his experience as Global Medical Director for Scientific Affairs, Women's Health and Immunology and other experience gained during his tenure with Organon.

I find that Dr. Rekers is qualified to offer expert testimony on these matters. Dr. Rekers has written on the relationship of second- and third-generation combined hormonal contraceptives and risk for VTE. (Doc. 1312, Exh. 5 at 6). While at Organon, Dr. Rekers was

responsible for managing product efficacy and safety issues, which included analyzing studies of NuvaRing and other hormonal contraceptives on the topics Plaintiffs challenge. I find that his knowledge of these areas is sufficient to assist the jury in its role as fact-finder. Plaintiffs' challenge of Dr. Rekers's testimony on these topics is denied**.**

f) Clinical trials and cumulative testimony

Plaintiffs allege that Dr. Rekers lacks qualifications to testify regarding clinical trials. Plaintiffs further argue that his testimony as to regulatory matters, hematology, pharmacology, epidemiology, biostatistics, obstetrics, and gynecological issues are cumulative to other testimony from Organon's experts. Each of these arguments was raised for the first time in Plaintiffs' reply brief. These challenges have not been properly raised in a timely Daubert motion. As a result, these arguments will not be considered.

IV. CONCLUSION

In sum, Plaintiffs' motions to exclude testimony of Defendants' experts Dr. Titia Mulders and Dr. Hans Rekers [Doc. #s 1313 & 1311] are **DENIED IN PART** and **GRANTED IN PART** as stated above.

RODNEY W. SIPPEL
UNITED STATES DISTRICT JUDGE

Dated this 4th day of March, 2013.